Claims

1. A purified and isolated non-naturally occurring nucleic acid ligand to a fibrillar protein target, wherein said ligand is an RNA ligand selected from the group comprising:

(i) the nucleic acid depicted in any one of SEQ ID NOS: 1-55 or 58 –105;

(ii) having the corresponding DNA or RNA sequences of any one of SEQ ID NOS: 1-55 or 58–105 or the corresponding fully complementary sequences thereof or their L-ribose derivatives;

(iii) derivatives of the sequence depicted in any one of SEQ ID NOS: 1-55 or 58 –105 having at least about 60%, 70%, 80% or 90% sequence identity to any one of the nucleotide sequences, and which have a binding affinity to a fibrillar protein.

2. The nucleic acid ligand according to claim 1 which is substantially homologous to and has substantially the same ability to bind said fibrillar protein target as a ligand selected from the group comprising the nucleic acids depicted in any one of SEQ ID NOS: 1-55 or 58 –105.

3. The nucleic acid ligand according to either preceding claim which has substantially the same structure and the same ability to bind said fibrillar protein target as a ligand selected from the group comprising the nucleic acids depicted in any one of SEQ ID NOS: 1-55 or 58 –105.

4. The nucleic acid according to any preceding claim wherein the fibrillar protein target is selected from the group comprising monomeric β2m or Aβ1-40 or Aβ1-42, protofibrillar β2m or Aβ1-40 or Aβ1-42, mature fibrillar β2m or Aβ1-40 or Aβ1-42.

5. The nucleic acid according to any preceding claim wherein the fibrillar protein target comprises either L- or D-amino acid molecules.

6. The nucleic acid according to any preceding wherein the nucleic acid of any one of SEQ ID NOS: 1 to 16 have a preferential binding affinity to a D-amino acid Aβ1-40 monomeric target.

7. The nucleic acid according to any one of claims 1 to 5 wherein the nucleic acid of any one of SEQ ID NOS: 17 to 36 have a preferential binding affinity to a D-amino acid Aβ1-40 pre-fibrillar target.

8. The nucleic acid according to any one of claims 1 to 5 wherein the nucleic acid of any one of SEQ ID NOS: 37 to 55 have a preferential binding affinity to a D-amino acid Aβ1-40 protofibril target.

9. The nucleic acid according to any one of claims 1 to 5 wherein the nucleic acid of any one SEQ ID NOS: 58 to 71 have a preferential binding affinity to a native β2-microglobulin protein target.

10. The nucleic acid according to any one of claims 1 to 5 wherein the nucleic acid of any one of SEQ ID NOS: 72 to 90 have a preferential binding affinity to a β2-microglobulin immature fibril protein target.

11. The nucleic acid according to any one of claims 1 to 5 wherein the nucleic acid of any one of SEQ ID NOS: 91 to 105 have a preferential binding affinity to a β2-microglobulin mature fibrillar protein target.

12. The nucleic acid according to any preceding claim further including any one or more of the following features:

(i) a fluorescent label;

(ii) an imaging label or;

(iii) a flanking region.

13. The nucleic acid according to claim 12 wherein the flanking region comprises any one or more nucleic acid sequences selected from the group comprising SEQ ID NOS: 56, 57, 106 and 107.

14. A vector comprising at least one or more nucleic acid as defined in any preceding claim.

15. A host cell including at least one or more nucleic acid as defined in any of claims 1 to 13 or the vector of claim 14.

16. Use of a binding motif comprising a peptide sequence derived from human β2m that retains the ability of the whole protein to form amyloid fibrils, as a target for selecting a nucleic acid ligand.

17. Use of a peptide sequence comprising any one of SEQ ID NO: 111, 112 or 113 or derivatives or variants thereof that retain the ability of the whole protein to form amyloid fibrils, as a target for selecting a nucleic acid ligand.

18. A purified and isolated non-naturally occurring nucleic acid ligand to a fibrillar protein target, wherein the target comprises a binding motif as defined in either claim 16 or 17.

19. A purified and isolated non-naturally occurring nucleic acid ligand to a fibril cross β-core protein target.

20. A pharmaceutical comprising at least one nucleic acid as defined in any one of claims 1 to 13 or the vector of claim 14.

21. A pharmaceutical according to claim 20 comprising a number of nucleic acid ligands each with binding affinities for the same or different forms of a fibrillar protein.

22. A pharmaceutical according to either claim 20 or 21 further including a suitable excipient, diluent or carrier.

23. Use of a nucleic acid according to any one of claims 1 to 13 for the manufacture of a medicament for treating amyloid diseases.

24. Use according to claim 23 for the treatment of Alzheimer's and DRA disease conditions.

25. A method of treating a patient suffering from Alzheimer's disease or a disease associated with amyloid formation comprising administering a therapeutically effective amount of a nucleic acid ligand according to any one of claims 1 to 13, or the vector of claim 14 or a pharmaceutical according to claims 20 to 22.

26. A method according to claim 25 wherein the therapeutically effective amount of a nucleic acid ligand or vector or pharmaceutical is administered by an intra-venous, intra-muscular, intra-peritoneal route and optionally is administered on more than one occasion.

27. Use of the nucleic acid according to any one of claims 1 to 13 or the vector of claim 14 as a diagnostic agent for detecting the presence and/or progression of an amyloid disease.

28. A method of monitoring the presence and/or progression of an amyloid disease comprising administering to a patient at least one nucleic acid according to any one of claims 1 to 13 or the vector of claim 14 or a pharmaceutical according to any one of claims 20 to 22 and imaging the presence of binding of said nucleic acid ligand to an amyloid fibril and optionally repeating the process at a later date to assess presence or progression of a disease state.

29. A method for the isolation of nucleic acid ligands to a fibrillar protein target comprising:

(i) preparing a candidate mixture of nucleic acids;

(ii) contacting the candidate mixture of nucleic acids with a biotinylated immobilised fibrillar protein on ice, wherein nucleic acids having an increased affinity to the fibrillar protein relative to the candidate mixture are partitioned from the remainder of the candidate mixture;

(iii) partitioning the increased-affinity nucleic acids from the remainder of the candidate mixture;

(iv) amplifying the increased-affinity nucleic acids to yield a mixture of nucleic acids with relatively high affinity and specificity for binding to the fibrillar protein, whereby a nucleic acid ligand of the fibrillar protein may be identified.

30. A method according to claim 29 wherein the candidate mixture comprises single stranded nucleic acids.

31. A method according to claim 30 wherein the single stranded nucleic acids comprise ribonucleic acids.

32. A method according to any one of claims 29 to 31 further including the step of modifying the nucleic acid ligand with a fluorescent label and/or an imaging reagent.

33. A method according to any one of claims 29 to 32 wherein the nucleic acid ligand further comprises a flanking selected from the group comprising SEQ ID NO: 56, 57, 107 or 108.

34. A nucleic acid product identified and isolated according to the method of any one of claims 29 to 33.